smoker) and smoking intensity (in pack-years) were asked at baseline. Radiographs and MRI films of knees were acquired at baseline and 30-, 60-, and 84-month visits. Kellgren & Lawrence (KL) grade was scored on posteroanterior knee radiographs and patellofemoral radiographic OA was scored on lateral view knee radiographs. A knee was considered as having whole knee radiographic OA (ROA) at baseline if it had either KL grade ≥2 or patellofemoral ROA. Incident whole knee ROA was defined among knees without whole knee ROA at baseline if the disease developed or new knee replacement surgery occurred during 84 months of follow-up. Cartilage morphology (CM) was scored on MRIs of one knee per subject using the Whole Organ Magnetic Resonance Score (WORMS). Cartilage lesions at baseline in the whole knee were defined as (1) any CM lesion: WORMS score ≥2 in any subregion, and (2) full thickness CM lesion: WORMS score 2.5 or ≥5 in any subregion. CM progression from baseline to 84-month visit was defined as at least a within-grade increase of WORMS score in any subregion. We examined the relation of smoking status and intensity to prevalent whole knee ROA at baseline with logistic regression, using generalized estimation equations to account for the correlation between two knees within a subject. We used the same approach to assess the effect of smoking on incident whole knee ROA. We used logistic regression to assess the relation of smoking to cartilage outcomes. The analysis of the relation of smoking to CM progression was repeated among knees without whole knee ROA at baseline. Baseline age, sex, race, clinic site, BMI, knee injury and surgery histories were adjusted for in all models.

Results: Among 3026 subjects recruited at baseline (age mean ±; SD: 62.5 ±; 8.1, BMI mean ±; SD: 30.7 ±; 6.0 kg/m^2, 60% women), 197 subjects (6.5%) were current smokers and 1155 (38.2%) were former smokers. The median (25th, 75th percentile) smoking intensity among smokers was 21.5 (15.0, 31.0) pack-years. The prevalence of whole knee ROA at baseline was 46%, 43%, 45% among never, current, and former smokers, respectively, and risks of incident whole knee ROA during 84-month follow-up were 25%, 23%, and 24%. There was no significant relation of smoking to prevalent and incident whole knee ROA, respectively (see table). Complete baseline CM scores were available among 1006 knees (age mean ±; SD: 60.9 ±; 7.5, BMI mean ±; SD: 29.4 ±; 4.6 kg/m^2, 62% women). The prevalence of any CM lesion at baseline was 71% among never smokers, and was not higher among current or former smokers with odds ratios (95% CI) 1.1 (0.5, 2.2) and 0.9 (0.7, 1.2), respectively (table). Similar results were found for the association between smoking and prevalence of full thickness cartilage lesion at baseline, as well as of CM progression. When limited to knees without whole knee ROA at baseline, the odds ratios (95% CI) of CM progression were 1.1 (0.5, 2.1) among current smokers and 1.0 (0.7, 1.3) among former smokers compared with never smokers. No relation was found between smoking intensity and radiographic OA outcomes as well as cartilage outcomes (table).

Conclusions: Smoking was not related to radiographic knee OA or to cartilage lesions in this community-based cohort of older adults.

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NOVEL METABOLIC MARKERS FOR CONCURRENCE OF OSTEOARTHRITIS AND DIABETES MELLITUS IDENTIFIED BY A METABOLOMICS APPROACH

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Purpose: Our previous study found that osteoarthritis (OA) consisted of metabolically distinct subgroups and one of the subgroups tended to have a high prevalence of metabolic diseases (BMJ Open 2014). The purpose of the current study was to identify novel markers for concurrence of OA and metabolic diseases by using a metabolomics approach.

Methods: Synovial fluid and plasma samples were collected from patients undergoing total knee joint replacements due to primary OA. Plasma samples of healthy controls were also collected. Medical information on hypertension, dyslipidemia, high-BMI and diabetes were obtained by self-administered questionnaires and confirmed by their medical records. Metabolic profiling was performed on all the collected samples using UPLC-MS coupled with mixed standards assay kits to identify novel markers for OA and concurrence of OA and metabolic diseases.

Results: 64 OA patients and 45 healthy people were included in the study. Mean age were 65.6 ± 7.0 and 48.6± 6.3 years, respectively, and the mean BMI were 33.9 ± 7.3 and 30.1±6.7 kg/m2, respectively. 168 metabolite concentrations, including 40 acylcarnitines (including free carnitine), 20 amino acids, 9 biogenic amines, 87 glycerophospholipids, 11 sphingolipids and 1 hexose (>90% glucose), were quantified separately in synovial fluid and plasma samples. OPLS-DA analysis showed that diabetes OA patients could be clearly separated from non-diabetes OA patients based on synovial metabolite concentrations. Similar pattern was seen when plasma metabolite concentrations were used. 13 differential metabolites were identified between diabetes and non-diabetes OA patients from synovial analysis, of which 11 metabolites were the same as the differential metabolites identified in plasma analysis. The comparisons of these 11 metabolite plasma concentrations between diabetes OA, non-diabetes OA, and healthy controls found that 5 metabolic markers, citrulline, arginine, leucine, PC ae C34:3 and PC ae C36:3, were statistically and significantly different between these three groups with a linear trend (all $p < 0.003$). Leucine has been associated with knee OA in our previous study (ARD 2010). In addition, 3 metabolite concentrations, proline, alanine and acetyornithine, were statistically different between diabetes OA patients and healthy controls ($p < 0.0001$).

Conclusions: We confirmed our previous findings and further identified 7 novel metabolic markers for OA and concurrence of OA and diabetes mellitus, suggesting OA may have different pathogenesis when concurring with diabetes mellitus.

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SERUM BONE METABOLIC MARKER AFFECTS THE LUMBAR OSTEOARTHRITIS IN A JAPANESE POPULATION STUDY

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Purpose: To clarify the relationship between bone metabolic measurements (bone mineral density: BMD, serum biomarker) and the severity of lumbar osteoarthritis (LOA)

Methods: 689 volunteers participated in the present study (Male: 272, Female: 417, Age: 54.4±14.9, BMI: 23.0±3.3kg/m2). Lateral lumbar radiographs were evaluated in each intervertebral section (L1/2 to L5/S1) by Kellgren-Lawrence grade (KLG). If at least one intervertebral section was determined as KLG 2 or more severe, the subjects were defined as LOA. The summation of each section was determined as the severity score of LOA. BMD was evaluated by osteo-sono assessment index at the calcaneus bone. Blood samples were taken in early morning before breakfast. Serum bone alkaline phosphatase (BAP; μg/ml), N-telopeptide of typeI collagen (NTx; nMBCE/l), and pentosidine (Pen; nmol/l) were examined as the index of bone metabolism. Multiple linear regression analysis was conducted with the severity score of LOA as an independent variable, and age, sex, BMI, BMD, and the value of serum samples (BAP, NTx, Pen) as dependent variables.

Results: The total number of LOA subjects was 474 (68.5%). The frequency of LOA in males (n=199, 73.2%) was higher than that of females (n=273, 65.5%; P=0.036, $\chi 2$ test). The mean severity score of LOA was 7.1±4.4 in total subjects, 7.8±4.4 in male, and 6.8±4.4 in female (P=0.006, Mann-Whitney U test). The mean value of BMD was 2.7±0.4×106 in total subjects, 2.9±0.4×106 in male, and 2.5±0.3×106 in female (P<0.001, Mann-Whitney U test). The mean value of BAP

Table 1
Comparison of demographic data, bone mineral density, the severity of lumbar osteoarthritis, and serum bone metabolic markers between males and females

	Total	Male	Female	P-value
Age	54.4 ± 14.9	53.3 ± 15.3	55.2 ± 14.7	0.121
BMI	23.0 ± 3.3	23.7 ± 3.1	22.6 ± 3.3	<0.001*
BMD	2.6 ± 0.4	2.9 ± 0.4	2.5 ± 0.3	<0.001*
LOA	7.1 ± 4.4	7.7 ± 4.4	6.8 ± 4.4	0.006*
BAP	15.4 ± 11.8	15.8 ± 15.8	15.2 ± 8.2	0.770
NTx	18.7 ± 8.7	19.0 ± 10.7	18.5 ± 7.1	0.663
Pen	120.7 ± 54.8	132.7 ± 50.2	112.9 ± 56.2	<0.001*

BMD: bone mineral density (osteo-sono assessment index), LOA: the summation of Kellgren-Lawerence grade in each intervertebral section (L1/5 to L5/S1) with lateral X-ray image, BAP: bone alkaline phosphatase (μg/ml), NTx: N-telopeptide of type I collagen (nMBCE/l), Pen: pentosidine (nmol/l)

* P<0.05, Mann-Whitney U test.